

REMARKS

Claims 20-22, 28-29, and 31-32 were pending in the application. Claims 20, 21, and 31 have been amended without any intent of disclaiming equivalents thereof. Claims 28, 29, and 32 have been canceled without prejudice. New claims 33-47 have been added. Accordingly, upon entry of this paper, claims 20-22, 31, and 33-47 are pending and presented for consideration.

Support for the new claims is found in the specification as originally filed, at least at page 5, lines 14-15, page 9, lines 2-3, and page 13, lines 7-8 and 17-25. Support for claim amendments is found in the specification as originally filed at least at page 4, lines 4-12, page 6, line 27, to page 7, line 1, page 9, lines 1-3, and page 13, lines 26-32. Applicants respectfully submit that the amendments do not introduce new matter and that they are made without any intention to abandon the subject matter as filed, and with the intention that claims of the same, greater, or lesser scope may be filed in a continuing application.

Objections to the Specification

As requested by the Examiner, Applicants have amended the specification to update the status of the parent application U.S. Serial No. 08/978,285. Applicants have also deleted the paragraph at page 4, lines 13-14, which the Examiner found improper. Applicants respectfully request that the objections be withdrawn.

Rejection Under 35 U.S.C. §102(b) over Griffin et al.

The Examiner rejected claims 20-22 and 31 under 35 U.S.C. §102(b), contending that they are anticipated by Griffin et al. (WO 93/01209). Applicants traverse the rejection to the extent it is maintained over the claims as amended.

Anticipation under 35 U.S.C. §102 requires that all of the elements and limitations of the claims at issue be found within a single prior art reference. *Carella v. Starlight Archery and Pro Line Co.*, 804 F.2d 135, 231 U.S.P.Q. 644 (Fed. Cir. 1986).

Griffin *et al.* does not teach all the elements and limitations of Applicants' claims. Amended claim 20 relates to a kit for assaying free protein S that comprises a ligand comprising an amino acid sequence homologous or analogous to the extreme N-terminal SCR-module of the β -chain of the C4BP molecule and a reagent other than protein S comprising at least one of an antibody specific for protein S, a fragment thereof, and an indicating means capable of producing a detectable signal indicative of the formation of a complex between free protein S and the ligand. By contrast, Griffin *et al.* uses a labeled protein S polypeptide in a competition reaction assay in which an indicating means detects the formation of a complex between the labeled competing protein S polypeptide and the ligand, not the formation of a complex between free protein S in a sample and the ligand. Thus, contrary to Applicants' claims, Griffin *et al.* uses a protein S polypeptide to bind to C4BP and inhibit the binding of free protein S to C4BP, rather than use a reagent that is other than protein S to detect the formation of a complex between free protein S and C4BP. See, WO 93/01209, page 51, lines 7-9. "The competition reaction admixture is then maintained for a time period sufficient for the polypeptide and the PS_F present in the liquid phase to compete for binding with the solid phase C4BP. . . . and resulting in the formation of an indicating means-containing reaction product comprising the labeled polypeptide complexed with C4BP in the solid phase." See, WO 93/01209, page 51, lines 19-28. Therefore, Applicants submit that Griffin *et al.* does not disclose each and every element of the invention claimed in Applicants' amended claim 20. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claim 20 and the claims depending from claim 20.

Amended claim 31 relates to a composition for purifying free protein S from an aqueous solution comprising a ligand comprising an amino acid sequence homologous or analogous to the extreme N-terminal SCR module of the β -chain of the C4BP molecule and at least one further

reagent for purification of protein S, wherein the at least one further reagent is capable of releasing free protein S from a complex comprising free protein S and the ligand. Applicants submit that Griffin *et al.* does not disclose a composition for purifying free protein S comprising a reagent that is capable of releasing protein S from the free protein S/ligand complex and therefore does not disclose Applicants' claimed invention. Applicants therefore respectfully request reconsideration and withdrawal of the rejection of claim 31 and the claims depending from claim 31.

Rejection Under 35 U.S.C. §102(b) over Hardig *et al.* (1996) *J. Biol. Chem.* 271:20861-20867

The Examiner rejected claims 20-22 and 31 under 35 U.S.C. §102(b), contending that they are anticipated by Hardig *et al.* (1996) *J. Biol. Chem.* 271:20861-20867. Applicants traverse the rejection to the extent it is maintained over the claims as amended.

Hardig *et al.* does not disclose each and every element of Applicants' invention. Amended claim 20 recites a reagent other than protein S comprising at least one of an antibody specific for protein S, a fragment thereof, and an indicating means capable of producing a detectable signal indicative of the formation of a complex between free protein S and the ligand. Hardig *et al.* teaches direct binding assays and competition assays for testing the binding between protein S and intact C4BP or chimeric C4BP using ¹²⁵I-labeled protein S so that the amount of bound protein S can be measured in a -counter. See, e.g., Hardig *et al.*, page 20864, left column. Hardig *et al.* does not teach or suggest a reagent other than protein S comprising an indicating means, as required by amended claim 20, and therefore does not disclose Applicants' claimed invention. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claim 20 and the claims depending from claim 20.

Regarding claim 31, Applicants submit that Hardig *et al.* does not disclose a composition for purifying free protein S comprising a reagent that is capable of releasing protein S from the free protein S/ligand complex and therefore does not disclose Applicants' claimed invention.

Application Serial No.: 10/037,296

Response dated April 19, 2004

Reply to Office Action of December 19, 2003

Page 9 of 12

Applicants therefore respectfully request reconsideration and withdrawal of the rejection of claim 31 and the claims depending from claim 31.

Rejections Under 35 U.S.C. §103(a) over Hardig et al. in view of Griffin et al.

The Examiner rejected claims 20-22 under 35 U.S.C. §103(a), contending that they are unpatentable over Hardig *et al.* (1996) J. Biol. Chem. 271:20861-20867 in view of Griffin *et al.* (WO 93/01209). Applicants traverse the rejection to the extent it is maintained over the claims as amended.

The proper standard for evaluating obviousness requires a determination of (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process; and (2) whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success. *See In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991). Both the suggestion and the reasonable expectation of success must be found in the prior art, not in Applicant's disclosure. *See id.* citing *In re Dow Chemical Co.* 837 F.2d 469, 473, 5 U.S.P.Q.2d 1529, 1531 (Fed. Cir. 1988). Finally, section 103 requires that the suggestion or incentive to combine prior art references must be derived from the teachings of the references. *See ACS Hosp. Systems, Inc. v. Montefiore Hosp.* 732 F.2d 1572, 1577, 21 U.S.P.Q. 929, 933 (Fed. Cir. 1984).

Applicants submit that there is no motivation in either Hardig *et al.* or Griffin *et al.* to combine their disclosures to make Applicants' claimed invention and even if, *arguendo*, such motivation were found and the disclosures of the references were combined, such a combination would not teach Applicants' invention. Hardig *et al.* does not disclose a reagent other than protein S comprising at least one of an antibody specific for protein S, a fragment thereof, and an indicating means capable of producing a detectable signal indicative of the formation of a complex between free protein S and the ligand. Griffin *et al.* does not correct the deficiency of Hardig *et al.* Griffin *et al.* discloses a competition reaction assay for determining free protein S in a vascular fluid sample using a labeled competing protein S polypeptide. Therefore, Griffin *et al.*

teaches an indicating means that is indicative of the formation of the competing polypeptide/ligand complex not the formation of the free protein S/ligand complex. Therefore, even if the disclosures of Hardig *et al.* and Griffin *et al.* were combined, such a combination would not teach Applicants' claimed invention. Applicants therefore respectfully request reconsideration and withdrawal of the rejection of claims 20-22.

Rejection Under 35 U.S.C. §102(b) over Hillarp *et al.* (1988) J. Biol. Chem. 263:12759-12764

The Examiner rejected claim 20 under 35 U.S.C. §102(b), contending that it is anticipated by Hillarp *et al.* (1988) J. Biol. Chem. 263:12759-12764. Applicants traverse the rejection to the extent it is maintained over the claim as amended.

Hillarp *et al.* does not disclose each and every element of Applicants' invention. Amended claim 20 recites a reagent other than protein S comprising at least one of an antibody specific for protein S, a fragment thereof, and an indicating means capable of producing a detectable signal indicative of the formation of a complex between free protein S and the ligand. Hillarp *et al.* teaches protein S ligand blotting assay using ¹²⁵I-labeled protein S. See, e.g., Hillarp *et al.*, page 12762, left column. Hillarp *et al.* does not teach or suggest a reagent other than protein S comprising an indicating means as required by amended claim 20 and therefore does not disclose Applicants' claimed invention. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claim 20.

REQUEST FOR TELEPHONIC INTERVIEW

Applicants respectfully request a telephonic interview in order to expedite the prosecution of the claims. The Examiner is invited to telephone the undersigned at 617-310-8168 to arrange a convenient time to discuss any outstanding issues, and to work with the Examiner toward placing the application in condition for allowance.

CONCLUSION

Applicant respectfully urges that all claims are in condition for allowance and requests prompt and favorable action on the instant application.

Date: April 19, 2004
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Respectfully submitted,



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